

PROCESS FOR CONTROLLING THE HYDRATE MIX OF A COMPOUND

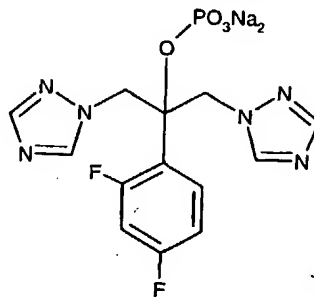
This application claims priority from U.S. Provisional Application Serial No. 60/399,491 filed 29 July 2002, which claims priority from United Kingdom Patent Application Number 0216515.7, filed 16 July 2002, which are hereby incorporated by reference in their entireties.

Field of the Invention

This invention relates to a process for controlling the hydrate mix of a compound, or a composition comprising the compound, the compound being capable of forming a plurality of hydration forms of differing stability. More particularly, this invention relates to a process for controlling the hydrate mix of a compound, or a composition comprising the compound, the compound being capable of forming a plurality of hydration forms of differing stability and also of dissolution to give a solution that, when frozen below the eutectic point, is a eutectic mixture.

Summary of the Invention

An example of a compound which exhibits a plurality of hydration forms is the disodium salt of fosfluconazole (hereinafter DSFF). DSFF is disclosed in WO97/28169 and has the following structure:



with
hydrate
tri + monohydrates

A number of hydration states of DSFF have now been found to exist and it is hypothesised that these are the dodecahydrate (33.4% w/w water), hexahydrate (20.1% w/w water), trihydrate (11.2% w/w water) and monohydrate (4.0% w/w water) forms. The anhydrous form of DSFF is believed to be amorphous. While the tri- and hexahydrate forms of DSFF are both chemically and thermally stable, it has been found that certain hydrate forms, such as the dodecahydrate, exhibit physical and/or chemical instability. While not wishing to be bound to any particular theory, it is believed that the eutectic form of DSFF is a dodecahydrate and it has been found that this dodecahydrate form is thermally unstable. Furthermore, it has been discovered that forms of DSFF which have a water content of from 4.0% w/w to 11.2% w/w are also chemically unstable. It is hypothesised that such a hydrate mix is a combination of tri- and monohydrate forms. Additionally, it has been found that samples of DSFF having a water content above the hexahydrate stoichiometry (20.1% w/w) collapse in a manner consistent with equilibration to the hexahydrate and water. Indeed, any composition comprising an unstable hydrate form, despite possibly containing stable forms, will decompose.